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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/726,366	SOTO-JARA, CLAUDIO	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,15-18 and 22-24* is/are pending in the application.

4a) Of the above claim(s) *1-11,13,14,19-21,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,15-18 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-26* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/3/03; 12/20/04; 1/18/05; 8/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 23 August 2005 has been entered in full. Claims 3 and 12-13 are amended. Claims 15-26 are added.

Election/Restrictions

Applicant's election without traverse of Group VI, claim 12, drawn to a method for reducing the formation of amyloid or amyloid like deposits involving abnormal folding into β sheet structure of amyloid β peptide comprising bringing into the presence of said amyloid β peptide an effective amount of an inhibitory peptide in the reply filed on 23 August 2005 is acknowledged.

Claims 1-11, 13-14, 19-21, and 25-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 23 August 2005.

Claims 12, 15-18, and 22-24 are under consideration in the instant application.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 03 December 2003, 20 December 2004, 18 January 2005, and 23 August 2005 have been considered by the examiner. However, the information disclosure statement filed 18 January 2005 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language (see for example, foreign patent document DE 19735902). It is also noted patents U.S. 5,948,763 and

6,462,171 have been crossed off of the IDS of 20 December 2004 because they were cited in duplicate.

Specification

1. The abstract of the disclosure is objected to because:

1a. The abstract is more than one paragraph in length. Correction is required. See MPEP § 608.01(b).

1b. Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Complete revision of the content of the abstract is required on a separate sheet.

Claim Objections

2. Claim 17 is objected to because of the following informalities:

Claim 17 is missing a "." at the end of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 12, 15-18, and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a method for reducing the formation of amyloid or amyloid-like deposits or for reducing the amount of amyloid β peptide which has already formed into a beta sheet structure comprising administering an effective amount of a β-sheet breaker peptide analog designed by chemical modification of a β-sheet breaker peptide capable of inhibiting β pleated sheet formation in an amyloid β-peptide. The claims also recite that the β-sheet breaker peptide comprises iAβ5 (SEQ ID NO: 1). The claims recite that the inhibitor peptide analog has side-chain groups corresponding to amino acids Leu, Pro, Phe, Phe, and Asp. The claims disclose that the chemical modification is achieved by a process selected from the group consisting: of alteration of the N- and C-terminal ends of said inhibitory peptide; replacing at least one residue of the peptide iAβ5 with α-aminoisobutyric acid; modification of an α carbon of the peptide selected from the group consisting of methylation, alkylation, dehydrogenation, and combinations, thereof; amidation; replacement of an L-enantiomeric residue with a D-enantiomeric residue; head-to-tail cyclization of peptide; replacement of an amide bond in peptide with an amide bond surrogate; and combinations thereof.

The specification teaches a βsheet breaker peptide of SEQ ID NO:1 (iAβ5; Leu Pro Phe Phe Asp) that is chemically modified. However, the description of one βsheet breaker peptide species (SEQ ID NO: 1) is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate an infinite number of larger peptides and proteins comprising the short amino acid sequence of SEQ ID NO: 1. The description of one chemically

modified βsheet breaker peptide species (SEQ ID NO: 1) is also not adequate written description of an entire genus of chemically modified β-sheet breaker peptide analogs that inhibit β-pleated sheet formation in an amyloid β-peptide.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the encompassed peptides and proteins, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The peptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a 5 residue β-sheet breaker peptide of SEQ ID NO: 1 (Leu-Pro-Phe-Phe-Asp) that is chemically modified, but not the full breadth of the claim meets the written

description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 12 and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 12 and 15-18 are rejected as being indefinite because it is unclear of the meaning of the term "capable of" in claim 12, line 6. Does this term mean that the β-sheet peptide inhibits β pleated sheet formation in amyloid β-peptide all of the time? Or, part of the time? Or, only in the proper environmental conditions? (Please note that this issue could be overcome by amending line 6 of claim 12 to recite, for example, "...a β-sheet breaker peptide that inhibits β pleated sheet formation in an amyloid β-peptide".)

6. Claims 12 and 15-18 are rejected as being indefinite because it is unclear of the meaning of the term "designed by" in claim 12, line 6. The phrase "designed by chemical modification" could simply mean that the peptide is incubated in a different buffer. Additionally, it is not clear from the term "designed by" if the β-sheet breaker peptide is actually chemically modified. For example, a peptide analog may be designed or planned out on paper, but it is not clear how the peptide analog is "designed" in a test tube. (Please note that this issue could be overcome by

amending claim 12, line 6 to recite, for example, "a β-sheet breaker peptide analog generated by chemical modification...".)

7. Claim 16 recites the limitation "inhibitor peptide analog" in line 1. There is insufficient antecedent basis for this limitation in the claim. It is noted that claim 12, upon which claim 16 depends, does not recite the limitation "inhibitor peptide analog". If the limitation "inhibitor peptide analog" of claim 16 is intended to refer to "a β sheet breaker peptide analog", it is not clear to the Examiner how claim 16 differs in scope and content from claim 15.

8. Claims 12 and 15-18 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating a reduction in the formation of amyloid or amyloid-like deposits or a reduction in the amount of amyloid β peptide which has already formed into a beta-sheet structure.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claim 22 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 8 of U.S. Patent No. 5,948,763. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite a method for reducing the formation or amount of amyloid or amyloid-like deposits involving the abnormal folding of amyloid into a β-sheet structure comprising contacting the amyloid protein prior to or after the abnormal folding thereof into a β sheet structure with a means for reducing the formation or amount of an amyloid deposit. The patented species claims of methods of reducing the formation or amount of amyloid or amyloid-like deposits comprising contacting the amyloid protein with an inhibiting peptide comprising a portion of three to eight amino acids, which portion is hydrophobic and has one or more proline residues therein, said inhibitory peptide having a length of three to fifteen amino acids render obvious the pending genus claim of a method of reducing the formation or amount of amyloid or amyloid-like deposits comprising contacting the amyloid protein with any means for reducing the formation or amount of an amyloid deposit.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 12, 17-18, and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by being anticipated by Findeis et al. (WO 96/28471).

Findeis et al. teach a peptide that binds to natural β amyloid peptides and modulates the aggregation of natural β amyloid peptides (pg 3-6, 11). Findeis et al. also teach that the peptide may be modified at the amino terminus, carboxy terminus, or both, with such groups as amide groups, alkyl or aryl amide groups, and hydroxyl groups (pg 14, last paragraph through pg 15). Findeis et al. disclose that modifying groups can be attached to the peptidic component by standard methods, for example using methods for reaction through an amino group, a carboxyl group, a hydroxyl group, or other suitable reactive group on an amino acid side chain (pg 25, lines 37-38 through pg 26, lines 1-2; pg 30, lines 27-39). Furthermore, Findeis et al. teach a method for inhibiting the formation of natural β-amyloid peptide deposits comprising contacting the natural β-amyloid peptides with a modified modulator peptide such that aggregation of the natural β-amyloid peptides is inhibited (pg 6, lines 24-30; pg 37; pg 39, lines 8-36). Findeis et al. state that the method may be used to treat clinical occurrences of β amyloid deposition, such as Alzheimer's disease and Down's syndrome (pg 40, lines 11-20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Findeis et al. (WO 96/28471) as applied to claims 12, 17-18 and 22-24 above, and further in view of Soto et al. (Nat Med 4(7): 822-826, July 1998).

The teachings of Findeis et al. are set forth above.

Findeis et al. does not teach a β-sheet breaker peptide comprising iAβ5 (SEQ ID NO: 1). Findeis et al. does not teach a peptide analog that has side-chain groups corresponding to amino acids Leu, Pro, Phe, Phe, and Asp.

Soto et al. disclose the β-sheet breaker peptide of iAβ5 of SEQ ID NO: 1 of the instant application. Soto et al. teach *in vitro* and *in vivo* methods for reducing the formation of amyloid deposits or for reducing the amount of said amyloid β peptide which has already formed into a beta sheet structure comprising contacting the amyloid β peptide prior to or after the abnormal folding thereof into a β sheet structure with an effective amount of iAβ5 peptide (LPFFD; pg 822, 3rd full paragraph; pg 823, col 1).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method for reducing the formation of amyloid deposits comprising contacting the amyloid protein with chemically modified peptides as taught by Findeis et al. by utilizing the iAβ5 peptide as taught by Soto et al. The person of ordinary skill in the art would have been motivated to make that modification because amyloid beta protein plays role in the pathogenesis of Alzheimer's disease and chemically modified peptides have increased stability, bioavailability, and solubility (Findeis et al. pg 13, lines 13-15; Soto et al. pg 823, col 2). The person of ordinary skill in the art reasonably would have expected success because non-chemically modified 1Aβ5 reduced amyloid beta deposition *in vivo* (Soto et al.; pg 823, col 1)

and similar chemical modifications of peptides to increase stability, bioavailability, and permeability were already being performed at the time the invention was made (for example, Soto et al., pg 823, col 2). Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
09 November 2005

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER